UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,786	05/23/2001	Ronnie Palmgren	PU-0124	2351

22840 7590 11/17/2004

AMERSHAM BIOSCIENCES
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,786	PALMGREN ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the Office Action mailed on May 20, 2004 has been acknowledged. Currently, claims 1-20 are pending and under consideration.

Claim Objections

2. Claim 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 13 is recited as a independent product claim that should be written in independent form.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-11, 13-20 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6-15, 20-22,

25, 28 and 29, of copending Application No. 10/478,910 in view of Maggio et al (Enzyme-Immunoassay, Department of Pathology, Scripps Clinic and Research Foundation, May 14, 1987). The claims are drawn to a method of derivatizating the N-terminus or N-termini of one or more polypeptide or peptides with at least one acidic reagent containing a sulfonyl or sulfonic acid moiety coupled to an activated ester moiety to provide one or more peptide derivatives. The copending application only differs from the instant claims in not teaching that the peptide or polypeptide is immobilized to a solid support at least during step (a).

However, Maggio et al discloses that the advantage of a solid phase assay format is that washing can be carried out very easily by immersion and if microplates are used, they can be very convenient to wash thereby reducing labor in performing the assay (page 186).

It would have been obvious to one of ordinary skill in the art to modify the claimed method to include the use of a solid support because wash steps can be carried out easily thereby reducing labor in performing the assay. Further, performing solid phase assays are well known in the art.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-6 and 10-13 and 15-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Keough et al (WO 00/43792).

Keough et al anticipates the instant invention by teaching a method of identifying a polypeptide by derivatizing the N-termini of one or more peptides with one or more acidic moieties having a pKas of less than about 2 when coupled with the polypeptide or peptide to provide one or more derivatized analytes. This method is analyzed by mass spectrometric techniques to provide a fragmentation pattern (summary). Such mass spectral techniques include Electrospray Ionization (ESI) and Matrix Assisted Laser Desorption Mass Spectrometry (MALDI) (page 16, lines 16-35 and page 17, lines 15-30). The fragmentation pattern of the peptide is interpreted to sequence the polypeptide (page 7, lines 1-2). Thomas et al discloses coupling an acidic moiety reagent to the N-terminus of a cysteine-containing peptide, followed by oxidation to produce peptides containing two acidic moieties (sulfonic acids). The preferred acidic moieties are 2-sulfoacetyl, 2-sulfobenzoyl and 3-sulfopropionyl moieties (page 9, lines 1-15). These preferred acidic moieties are sulfonyls coupled to an ester moiety such as sulfosuccinic anhydride, and 2-sulfobenzoic acid cyclic anhydride and others (page 9, lines 1-30). The peptides are accurately determined using software that accepts mass spectral fragmentation data (page 18, lines 15-22). The polypeptide can be obtained by enzymatic digestion using trypsin, or chymotrypsin (page 8, lines 3-12). Keough et al also teaches kits with one or more acidic moiety reagents having Pkas less than about 2 when coupled with the polypeptide or one or more peptides. One or more buffer

systems used to facilitate derivatization of peptides are also included in the kit of the present invention wherein buffer systems used is dependent on the acidic moiety reagent included (page 23, lines 1-35). Keough et al is silent with respect to the half-life of the acid reagent not being less than 10 minutes, however, it is the Examiner's position that this teaching is inherent to what the instant reference teaches. Keough et al teaches the acid reagents utilized in the instant invention, therefore these reagents will inherently exhibit a half-life in aqueous solution of not less than 10 minutes.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 13-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Little et al (USP6,322,970).

Little et al anticipates the instant reference by teaching reagents comprising a sulfonyl moiety coupled to an ester moiety and a reagent selected from the group consisting of 3-sulfopropionic N-hydroxysuccinimide esters (column 59, lines 65-67).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 7-9 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keough et al in view of Little et al (USP#6,322,970).

The teachings of Keough et al are set forth above and differ from the instant claims by not disclosing a sulfonyl group being coupled to a particular ester such as N-hyroxysuccinimide (NHS) ester.

However, Little et al discloses a process for determining the identity of a target polypeptide using mass spectroscopy (abstract). Little et al discloses that target polypeptides can be captured by conjugation to a solid support by immobilizing. The conjugation can be mediated through a linker such as a sulfo-N-hydroxysuccinimide (NHS) ester that facilitates conjugation of the polypeptide through it amino terminus. (column 55, lines 40-66, column 56, lines 1-20 and column 59, lines 30-66 and column 60, lines 1-26) Claim 12 recites a step of protecting lysine residues prior to derivatizing. Little et al discloses that the termini of a target polypeptide are more reactive than the amino acid side groups and therefore the amino acid residues should be blocked prior to performing the reaction of interest (column 60, lines 27-50).

It would have been obvious to one of ordinary skill in the art to modify the reference of Keough et al to couple an N-hydroxysuccinimide (NHS) ester to a sulfonyl group taught by Little et al to facilitate conjugation of peptides to a solid support which has the advantage of being manipulated so that reagents and undesirable reaction products can be washed from the remaining immobilized polypeptide, which can then be cleaved from the solid support and analyzed by mass spectrometry (column 60, lines 17-27).

Response to Arguments

12. Applicant's arguments filed August 20, 2004 have been fully considered but they are not persuasive:

13. Applicant argument that the reference of Keough et al does not teach sulfonyls coupled to an ester moiety, but teaches sulfonyl groups coupled to anhydride reagents. Applicant contends that anhydride reagents are not esters. Applicant's arguments are noted but not found to be persuasive.

In response, although the anhydride reagents recited by Keough are not esters; a sulfonyl group coupled to an ester is found within the 3-sulfopropionic anhydride structures, (see example 8, page 14) and as evidenced by applicant's instant specification on page 23 which describes the synthesis of a NHS ester from a 3-sulfopropianic anhydride. Although the reference of Keough et al did not synthesize an NHS ester from 3-sulfopropionic anhydride, it is apparent that an ester coupled to a sulfonyl group is within the structure of the 3-sulfopropionic anhydride. The instant claim 1 calls for at least one acidic reagent containing a sulfonyl moiety coupled to an ester moiety, therefore, Keough satisfies the limitation of claim 1.

14. Applicant asserts that the benefits of the instant invention resides in the fact that all the step can be carried out under aqueous conditions making it amenable to automation, versus the previous technology which requires dry-down steps. This

assertion is noted but not found persuasive because these benefits are not found in the claims. Therefore, the reference of Keough et al apply to the instant claims.

15. Applicant argues that the reference of Little et al does not teach or even suggest a reagent which can be utilized in a method of identifying a polypeptide or suitable for use in peptide derivatization in an aqueous solution as recited in claims 13-14. This argument is noted but not found to be persuasive.

In response to applicant argument, the examiner views claims 13-14 as independent claims reciting a reagent. Claims reciting a reagent are considered to be product claims. Product claims are not given patentable weight for intended use. The reference of Little et al recites the instant reagents of claims 13-14 and therefore satisfies the limitations of the instant claims. Further, claim 13 appears to depend from a method claim, however, it is claimed as a product, which does not further limited the claimed method (see above objection). Claim 13 has also been rejected as an independent product under 102 and as part of a method claim under 103.

16. Applicant argument that the references of Keough et al and Little et al does not disclose or suggest derivatization of the peptides in aqueous solution. This argument is noted but not found to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.

1986). Keough et al teaches derivatization in an aqueous solution, which are called for by the instant claim 1 (see page 5, lines 11-12). The reference of Little et al was relied on for its teaching of a particular (NHS) ester group, which discloses that (NHS) esters facilitate conjugation of the polypeptide to a solid support during the method of derivatization of the polypeptide through its amino or carboxyl terminus. Although applicant contends that the instant invention is different from the prior art of Keough et al and Little et al, these differences do not appear in the claims. Therefore, it appears to the examiner that the combination of the references is proper.

Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah A. Davis
Remsen Bldg.
Room 3D58
November 8, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

11/12/04